



US005957915A

United States Patent [19] Trost

[11] Patent Number: **5,957,915**

[45] Date of Patent: ***Sep. 28, 1999**

[54] HAND-HELD LASER SCANNER

[75] Inventor: **David Trost**, San Francisco, Calif.

[73] Assignee: **Coherent, Inc.**, Santa Clara, Calif.

[*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: **08/898,719**

[22] Filed: **Jul. 22, 1997**

Related U.S. Application Data

[63] Continuation of application No. 08/377,131, Jan. 23, 1995, Pat. No. 5,743,902.

[51] Int. Cl.⁶ **A61B 17/36**

[52] U.S. Cl. **606/13; 606/11; 606/18**

[58] Field of Search 606/2, 4, 5, 6,
606/10, 11, 12, 13, 16, 17, 18

[56] References Cited

U.S. PATENT DOCUMENTS

4,492,230	1/1985	Sunago et al. .	
4,733,660	3/1988	Itzkan	606/9
4,887,019	12/1989	Reis et al.	606/4
5,125,923	6/1992	Tanner et al.	606/10
5,219,347	6/1993	Negus et al.	606/19
5,336,217	8/1994	Buys et al.	606/9
5,360,447	11/1994	Koop	623/15
5,364,390	11/1994	Taboada et al.	606/4
5,411,502	5/1995	Zair	606/10
5,480,396	1/1996	Simon et al.	606/4
5,533,997	7/1996	Ruiz	606/521
5,549,632	8/1996	Lai	606/5

FOREIGN PATENT DOCUMENTS

0 326 760	8/1989	European Pat. Off. .
0 714 642 A1	6/1996	European Pat. Off. .
0 724 866 A1	8/1996	European Pat. Off. .
WO 93/03521	2/1993	WIPO .

OTHER PUBLICATIONS

SHARPLAN SilkTouch™ Scanner User's Manual Prepared Oct. 1994, pp. 1-8.

SHARPLAN SWIFTLASE™ FLASHCAN Leaflet Cat. No. PB2344100, prepared Jun. 1993, pp. 1-6.

SHARPLAN 771B Laser Microscan User's Manual Prepared Jul. 1985, Laser Industries Ltd., pp. 1-29.

Copy of International Search Report, issued Jul. 5, 1996, in PCT/US96/01080, 5 pages.

Primary Examiner—John P. Leubecker

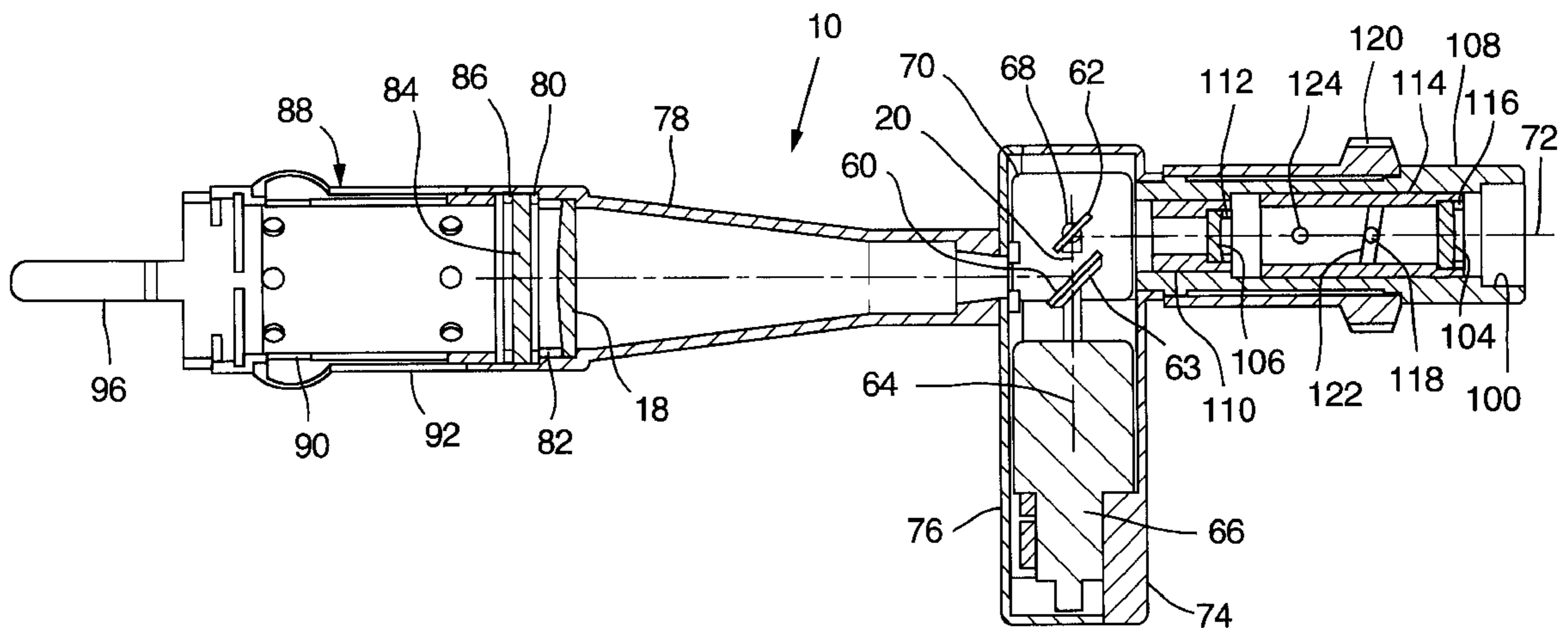
Assistant Examiner—Sonya C Harris

Attorney, Agent, or Firm—Limbach & Limbach L.L.P.

[57] ABSTRACT

A surgical laser scanner having optics that scans a pulsed laser beam onto a target tissue is disclosed. The laser scanner has a lens and a scanning mirror or mirrors located upstream of the lens at a distance substantially equal to the focal length of the lens. The laser beam hits the scanning mirror and is reflected onto the lens in a pattern defined by sequential positions of the scanning mirror. The laser beam is projected onto the target tissue by the lens in a direction parallel to the optical axis of the lens. The projected pattern has a constant size regardless of the distance between the laser scanner and the target tissue.

9 Claims, 7 Drawing Sheets



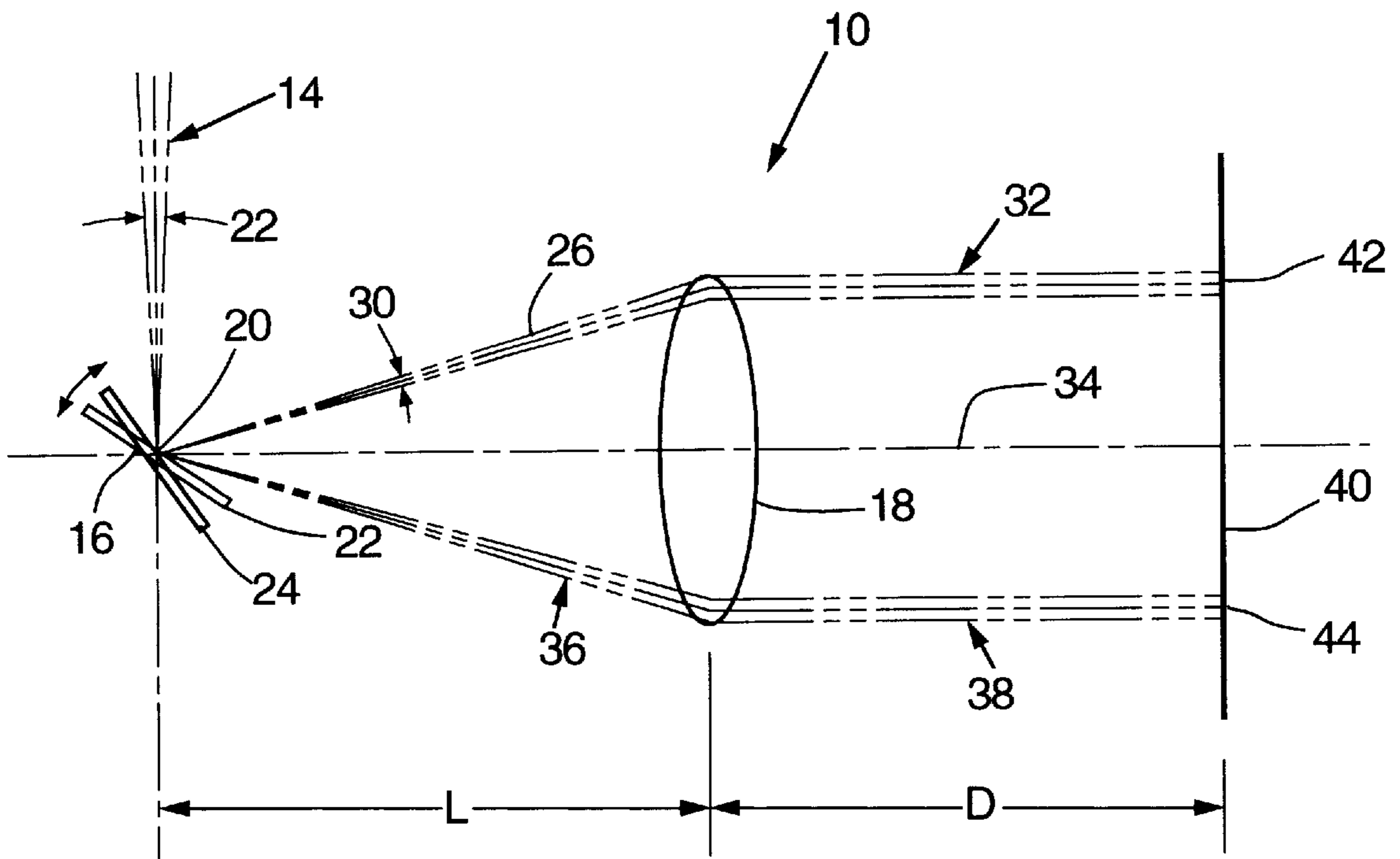


FIG. 1

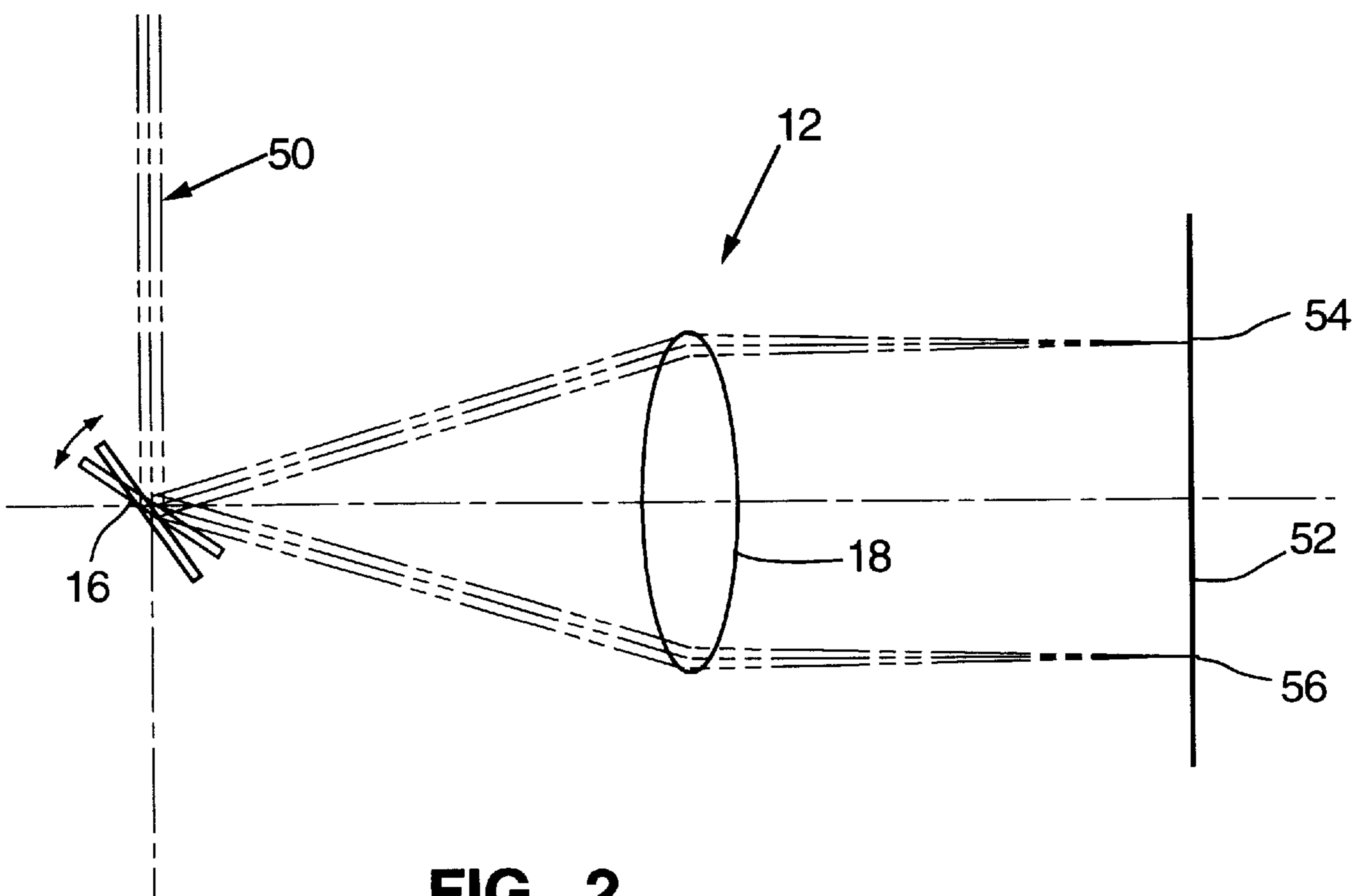


FIG. 2

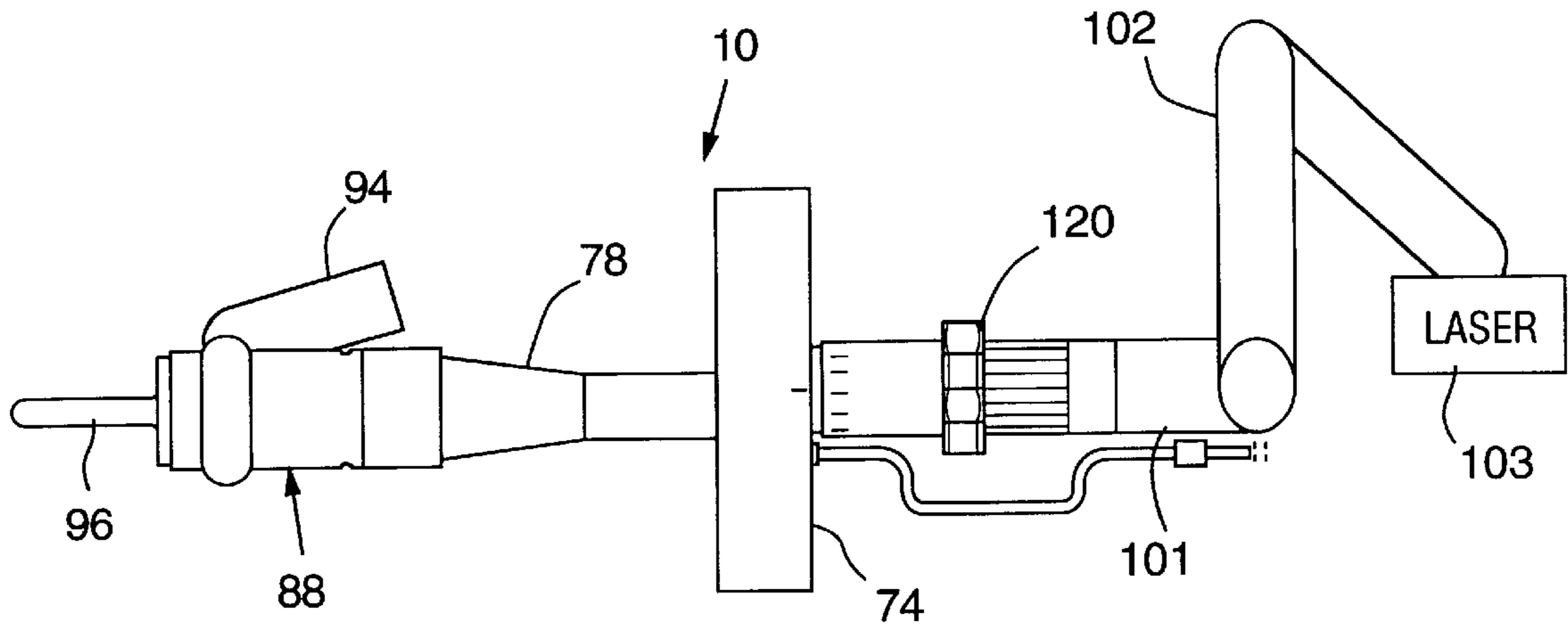


FIG. 3

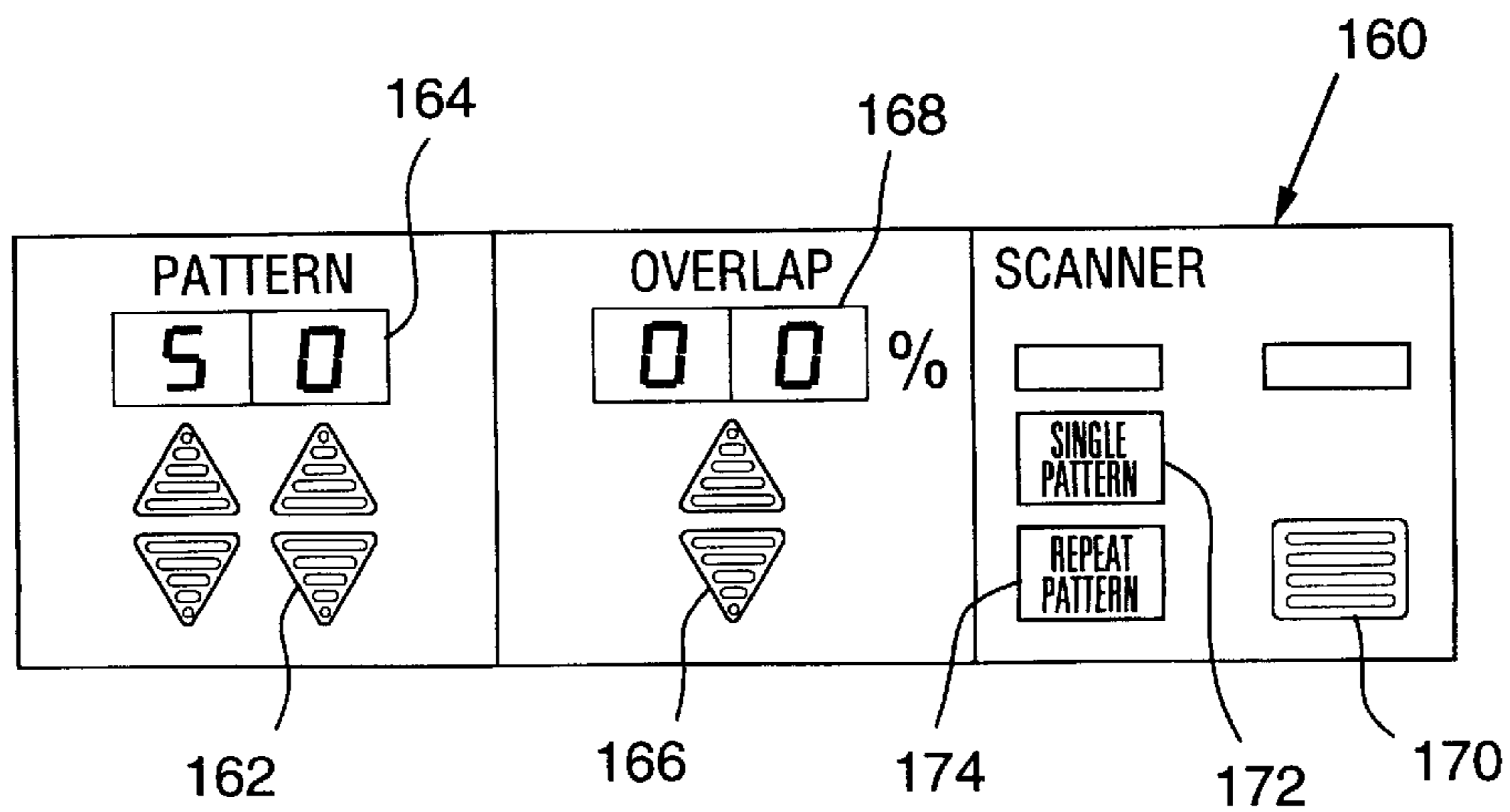
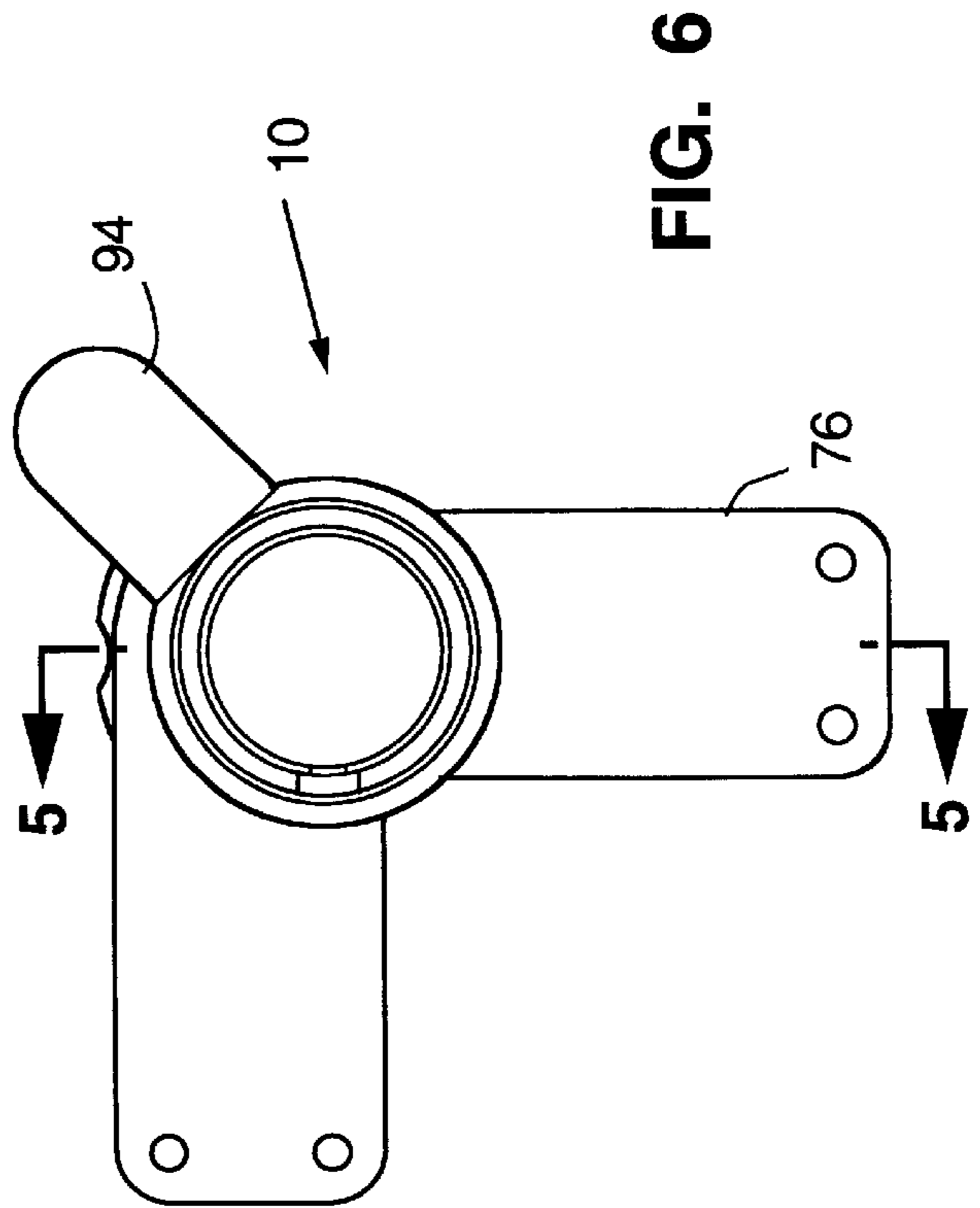
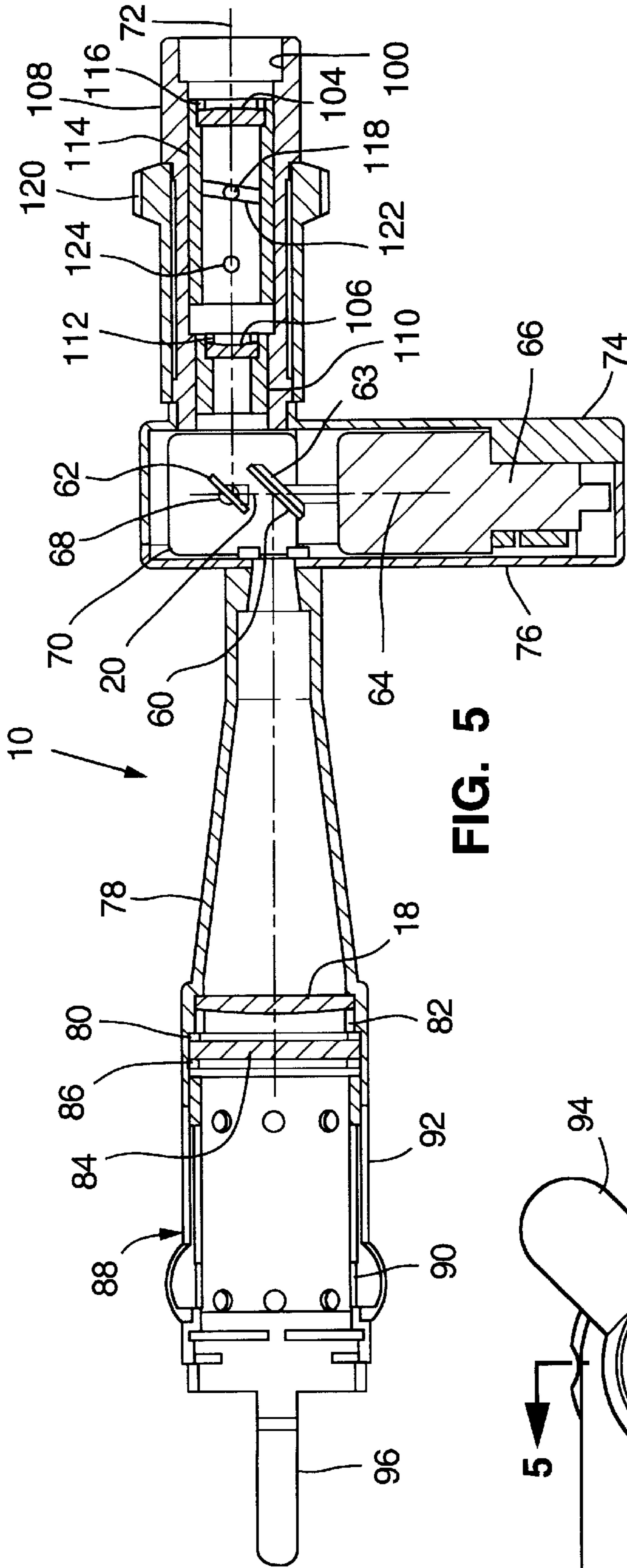
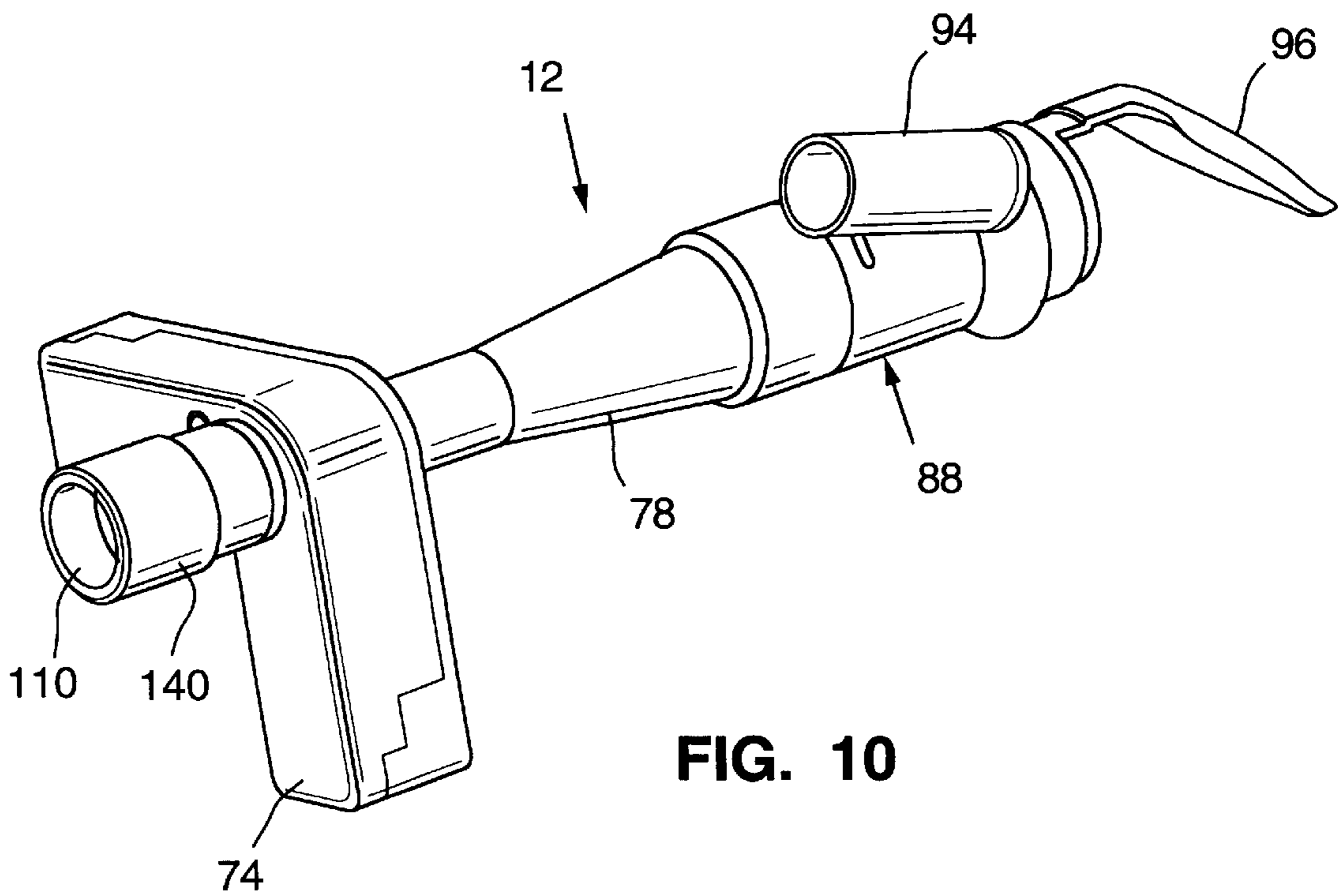
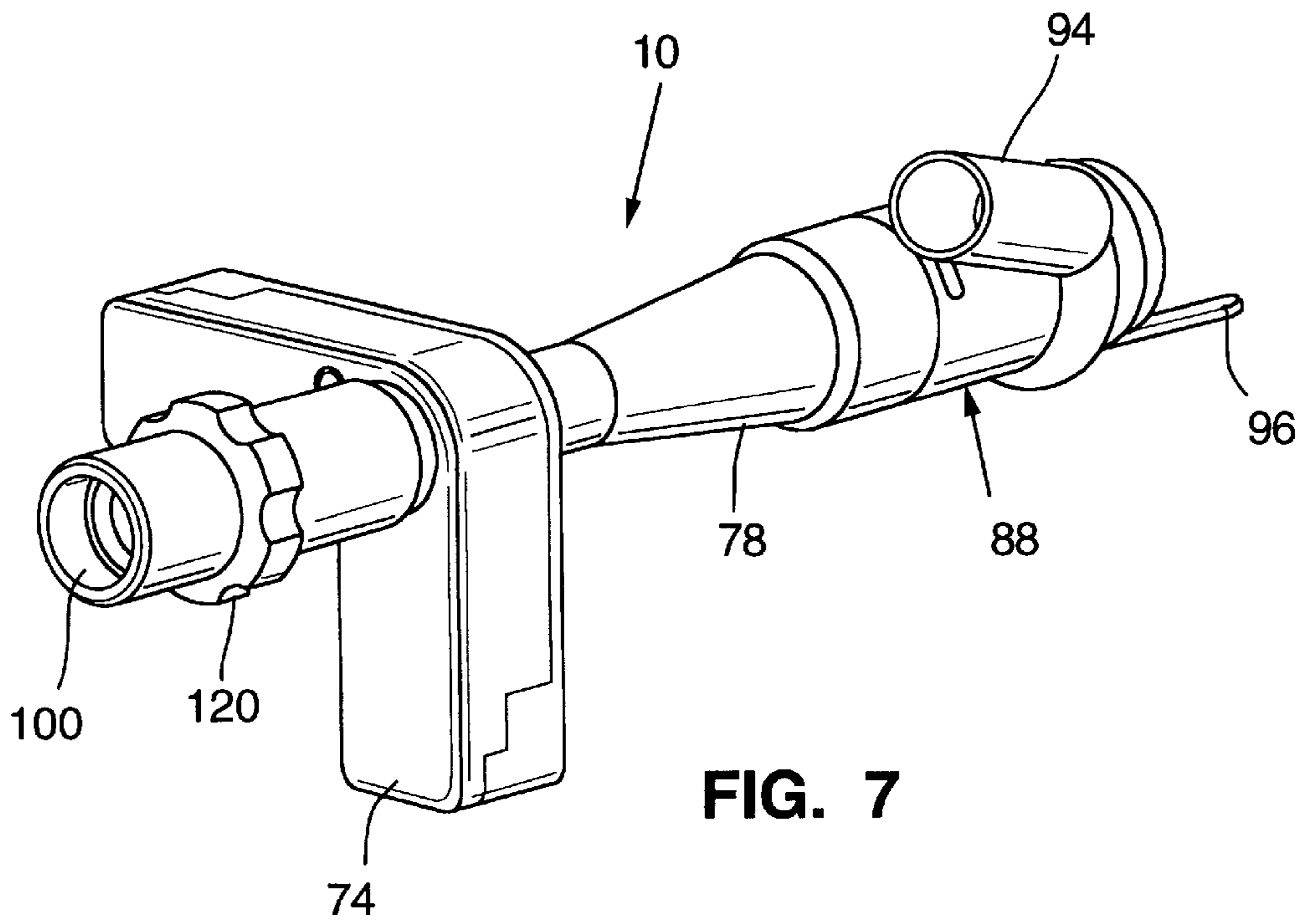


FIG. 4





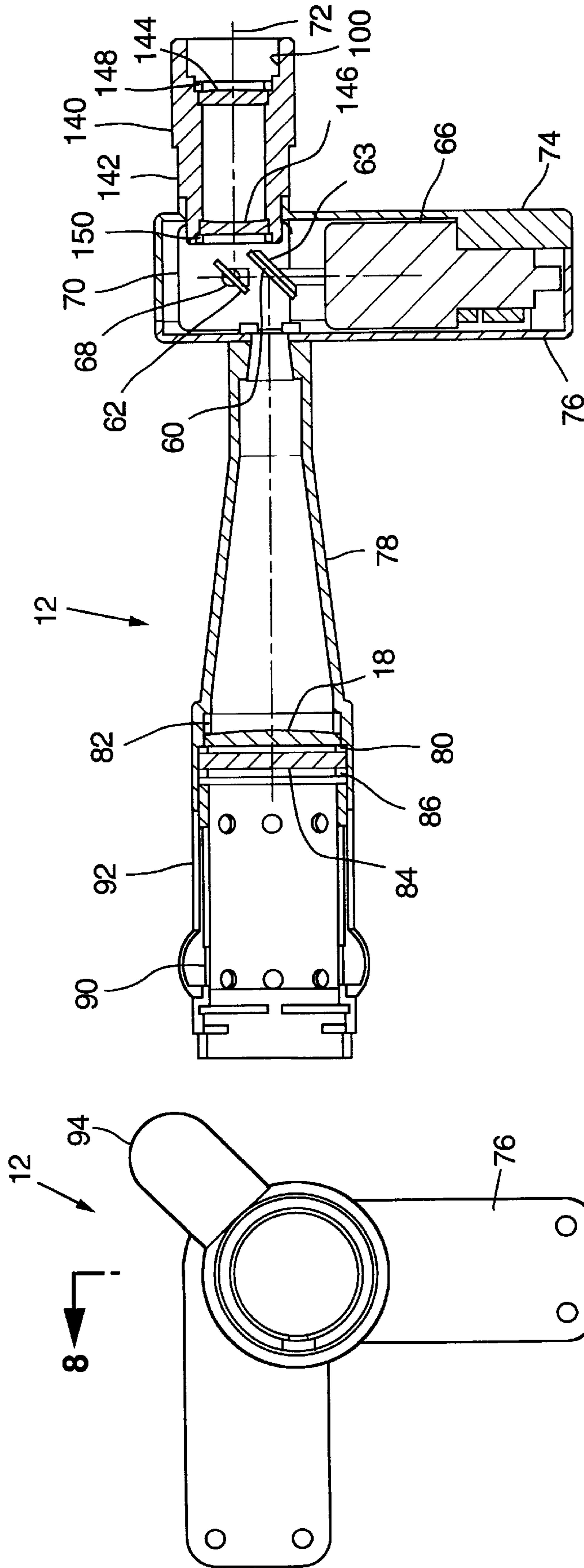


FIG. 8

FIG. 9

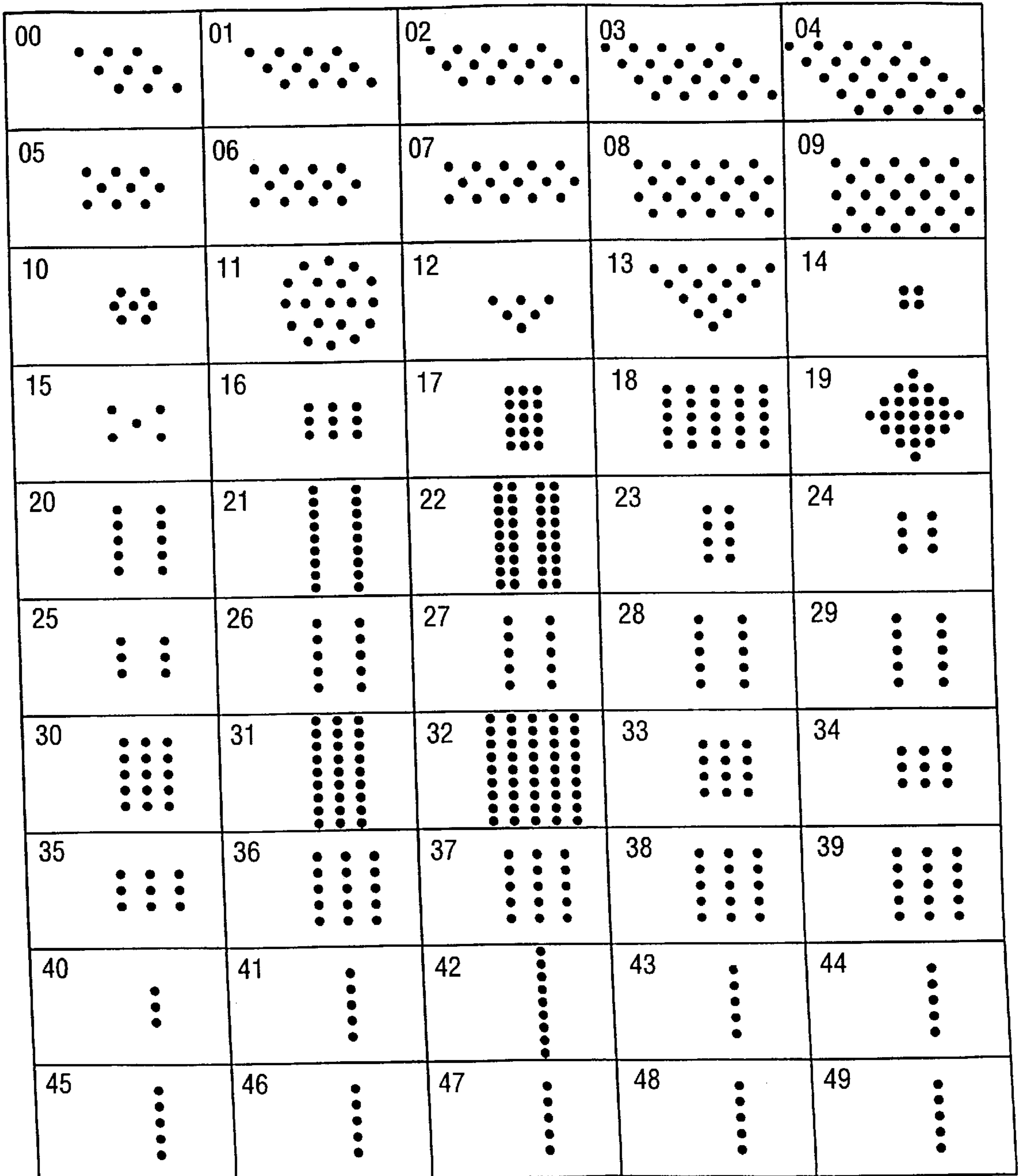


FIG. 11

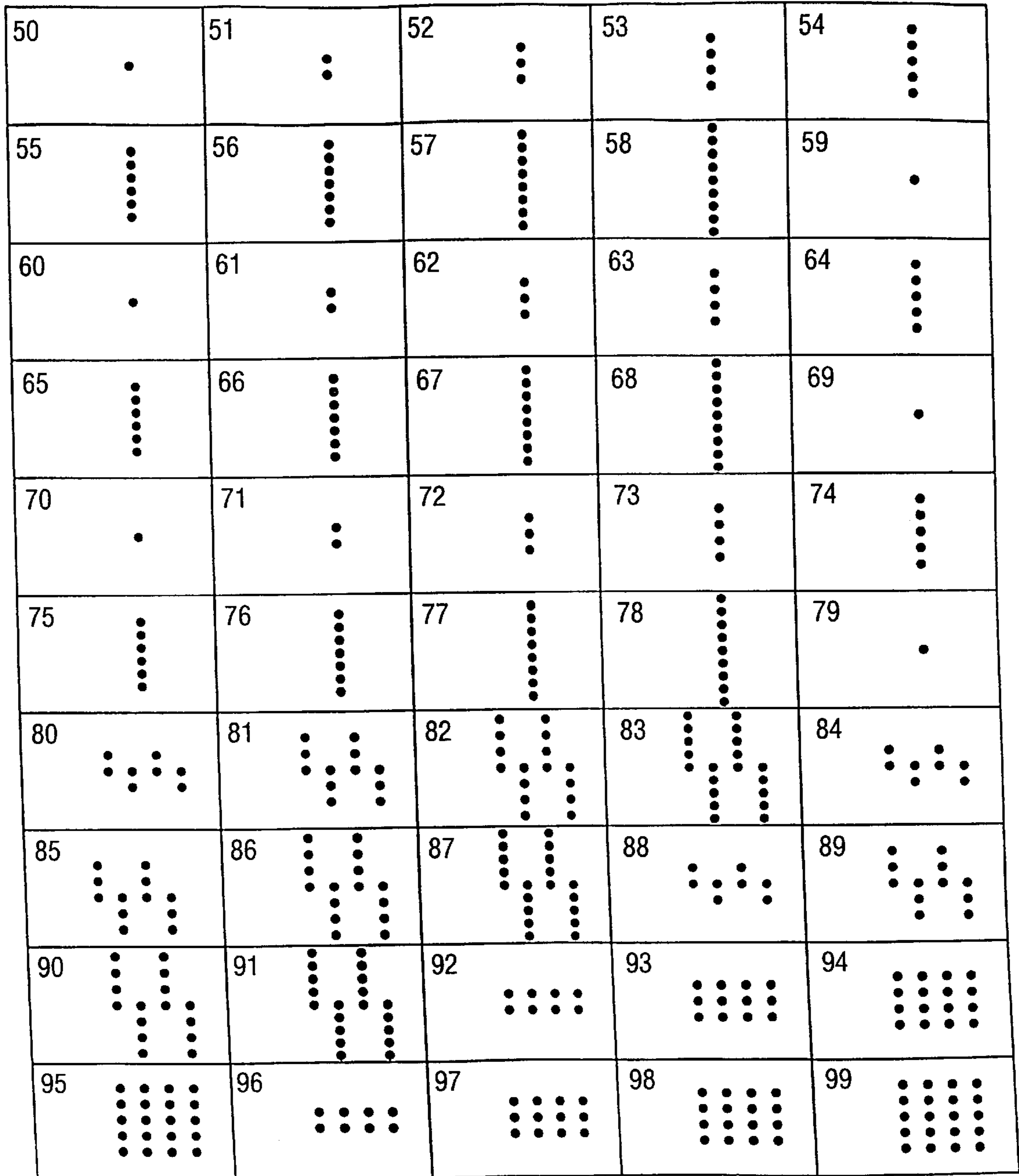


FIG. 12

HAND-HELD LASER SCANNER

This is a continuation of application Ser. No. 08/377,131, filed Jan. 23, 1995, now U.S. Pat. No. 5,743,902.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates generally to medical lasers, and relates more particularly to a hand-held laser scanner that generates a scanned pattern of constant size regardless of the positioning of the laser scanner with respect to a treatment surface.

2. Description of the Relevant Art

Historically, surgical incisions in tissue have been performed with sharp metal cutting instruments. More recently, lasers have become the tool of choice in many medical procedures to cut and treat tissue. Laser beams can be accurately focused on tissue to cut many desired shapes and depths. The slit incision, a very narrow elongated incision, is especially appropriate for laser surgery. Surgeons can make these narrow incisions by passing a focused laser beam over the target tissue.

One medical procedure where slit incisions are desired is hair transplants. Hair transplants have become a common cosmetic procedure, particularly for the treatment of male pattern baldness. In a hair transplant procedure, a piece of the patient's skin having healthy growing hair is removed from a donor region on the scalp and implanted into a hairless, recipient region. This process involves cutting a hole or slit into the recipient region so that the new plug of hair can be inserted. Slit grafting is modernly used because of its many cosmetic and medical advantages over circular punching.

Historically, slit grafting has been accomplished by cutting a slit into the recipient region with a scalpel. More recently, lasers have been used. A laser is more advantageous because the size and shape of the incision can be more accurately controlled. A laser beam, usually a pulsed infrared beam, is focused onto the scalp. The exposure can be controlled to remove the amount of skin needed for the hair graft dimensions. Another advantage of using lasers to cut or remove skin is the coagulating effects of the laser light that minimizes bleeding and pain. Further, the laser radiation removes the skin in the slit it creates thereby creating room for the new plug of hair to be placed inside. A laser assisted hair transplant method is described in U.S. Pat. No. 5,360,447, which is assigned to Coherent, Inc, the assignee of the present application.

A laser beam can be accurately focused on the scalp by a variety of optical delivery systems. One such system is marketed by Coherent, Inc. in conjunction with its sealed carbon dioxide medical laser system under the name Ultra-pulse 5000. To create a slit, the surgeon positions the output of the optical delivery system so that the beam will impinge on the target tissue. The surgeon then presses a footswitch which opens a shutter that allows light to exit the output end of the optical delivery system. The doctor then moves the output end over the target tissue until the desired slit width and depth is created. This procedure is followed for every slit made in the target tissue.

The drawback to this optical delivery system is that it takes time and skill to create a series of slits of the desired dimensions and layout. Since the number of slits required can be as numerous as the number of individual hair follicles being transplanted, the time and skill required to create

accurate slits in the recipient area can be great. Furthermore, the placement of each slit is important, because uniform patterns give a more natural appearance of the transplanted hair. Thus, there is a need for an optical delivery system that creates multiple slits in uniform patterns.

Lasers are also used surgically to treat relatively large areas of tissue in techniques such as ablation to remove disfigured skin. The spot diameter of the laser beam is typically larger in size and lower in power density as compared to lasers used to make incisions. Even though the spot diameter of the laser beam is relatively large, the area of treatment is usually larger than the area of the spot, which requires that the beam be scanned or otherwise moved across the area to be treated.

One approach to moving the laser beam across a treatment area is to scan the beam like a raster, back and forth in successive rows until the area is covered. One drawback to that approach is that successive rows can overlap with insufficient recovery time in between scans of successive rows, which can damage the tissue in the areas of overlap. Another drawback is that the pattern area covered by the laser can be dependent on the distance between the treatment area and the scanning device, which is not easily controlled if the laser instrument is handheld by the surgeon.

There is thus a need for an optical delivery system that creates an scanned laser beam in a uniform pattern regardless of the precise position of the treatment surface with respect to the laser instrument.

SUMMARY OF THE INVENTION

In accordance with the illustrated preferred embodiments, the present invention is a surgical laser handpiece that scans a laser beam onto a target tissue. The surgical handpiece, or hand-held laser scanner, has a lens and a scanning mirror located at a distance from the lens that is equal to or substantially equal to the focal length of the lens. The laser beam hits the scanning mirror and is reflected onto the lens in a pattern defined by multiple positions of the scanning mirror. The lens projects the laser beam pattern onto the target tissue so that the output beam exits the lens parallel to the optical axis of the lens. The projected pattern has a constant size regardless of the distance between the handpiece and the target tissue. In other words, any variation in the size of the pattern projected onto the target tissue is minimal as the spacing between the lens and the target tissue is varied.

In another aspect of the present invention, the laser beam incident on the scanning mirror can be focused light or collimated light. If the laser beam is focused on the scanning mirror, then the lens collimates the beam, resulting in an output beam having a spot size that does not vary with changing distance between the handpiece and the target tissue. The spot size of this output beam can be adjusted by varying the cone angle of the incident focused beam. If the laser beam incident on the scanning mirror is collimated, then the lens focuses the output beam, thus providing a concentrated laser beam useful for incisions. Beam conditioning optics located upstream of the scanning mirror can be used to focus the laser beam on the scanning mirror, to adjust the cone angle of the focused beam, and to adjust the size of the collimated laser beam incident to the scanning mirror. Preferably, the surgical handpiece of the present invention has two mirrors that are independently rotatable about orthogonal axes. The two independently rotatable mirrors permit two-dimensional patterns of the output beam to be generated.

Another aspect of the present invention is a method of scanning a laser beam onto a target tissue by generating a laser beam and delivering it to a scanning mirror, pivoting the scanning mirror to project the laser beam onto a lens, where the scanning mirror is one focal length upstream of the lens, and projecting the laser beam through the lens and onto the target tissue.

Still another aspect of the present invention is a method of ablating tissue using a laser beam by positioning an output end of a delivery device adjacent the tissue, energizing the laser to generate a laser beam, directing the laser beam within the delivery device through a scanning mirror and then a lens to the tissue, where the scanning mirror is located approximately one focal length from the lens so that the lens projects the laser beam along a path parallel to an optical axis of the lens, and moving the scanning mirror to project a pattern of laser beams on the tissue to be ablated.

The features and advantages described in the specification are not all inclusive, and particularly, many additional features and advantages will be apparent to one of ordinary skill in the art in view of the drawings, specification and claims hereof. Moreover, it should be noted that the language used in the specification has been principally selected for readability and instructional purposes, and may not have been selected to delineate or circumscribe the inventive subject matter, resort to the claims being necessary to determine such inventive subject matter.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic view of a scanning mirror that receives a focused laser beam and a lens that projects a pattern of collimated laser beams, which is used in one embodiment of a hand-held laser scanner according to the present invention.

FIG. 2 is a schematic view of a scanning mirror that receives a collimated laser beam and a lens that projects a pattern of focused laser beams, which is used in another embodiment of a hand-held laser scanner according to the present invention.

FIG. 3 is an overall view of a hand-held laser scanner according to the present invention.

FIG. 4 is a diagram of a control panel for the hand-held laser scanner.

FIG. 5 is a sectional view of the hand-held laser scanner of FIG. 1.

FIG. 6 is an end view of the hand-held laser scanner of FIG. 1.

FIG. 7 is a perspective view of the hand-held laser scanner of FIG. 1.

FIG. 8 is a sectional view of the hand-held laser scanner of FIG. 2.

FIG. 9 is an end view of the hand-held laser scanner of FIG. 2.

FIG. 10 is a perspective view of the hand-held laser scanner of FIG. 2.

FIG. 11 is a diagram of several scanning patterns utilized with the hand-held laser scanner of FIG. 1.

FIG. 12 is a diagram of several scanning patterns utilized with the hand-held laser scanner of FIG. 2.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

FIGS. 1 through 12 of the drawings depict various preferred embodiments of the present invention for purposes of

illustration only. One skilled in the art will readily recognize from the following discussion that alternative embodiments of the structures and methods illustrated herein may be employed without departing from the principles of the invention described herein.

The preferred embodiment of the present invention is a hand-held laser scanner or surgical handpiece that scans a laser beam in a uniform pattern over a target tissue. The theory of operation of the laser scanner 10, 12 can be explained by reference to FIGS. 1 and 2. In FIG. 1, an incident laser beam 14 is focused on a scanning mirror 16, which reflects the laser beam onto a lens 18. The scanning mirror 16 pivots so that the laser beam strikes the mirror at a point 20 that is one focal length L upstream of and along the optical axis of the lens.

The scanning mirror 16 moves between position 22 and position 24. At position 22, the mirror 16 reflects the laser beam to the top of the lens 18 along path 26. The angle 28 of the incident beam is the same as the angle 30 of the reflected beam along path 26 because the mirror 16 is a flat mirror. Each ray of the reflected beam is refracted by the lens 18 to a path 32 that is parallel to an optical axis 34 of the lens. The result is that the output laser beam is collimated and parallel to the optical axis 34.

When the scanning mirror 16 is at position 24, the incident laser beam 14 is reflected by the mirror to the bottom of the lens 18 along path 36. The lens refracts the laser beam to an output path 38 that is also parallel to the optical axis 34. The output laser beam is collimated because the beam incident on the lens 18 originates from the point 20, which is one focal length L from the lens.

The target tissue 40 is located at the output side of the lens 18. The two output beams 32 and 38 form a simple pattern of two spots 42, 44 on the target tissue 40. The position of the laser beam spots 42, 44 projected onto the target tissue 40 is a function of the mirror angle only. Positioning the scanning mirror 16 between position 22 and position 24 will result in spots in the pattern between spots 42 and 44. Note that the distance between the two spots 42, 44 does not vary with the separation distance D between the lens 18 and tissue 40. In other words, the size of the pattern of the projected laser beam spots is constant, regardless of the position of the target tissue relative to the laser scanner. Also, the size of the laser beam spots 42, 44 is constant regardless of the separation distance between the lens 18 and tissue 40 because the output beams are collimated.

The laser scanner 10 is hand-held by the operator, which makes it difficult to maintain a constant distance between the laser scanner and the target tissue without adding cumbersome jigs or support structures. The present invention eliminates concern over the separation distance D between the scanner and the target tissue because both the pattern area and the spot size are not affected by changes in the separation distance.

An alternative preferred embodiment of the present invention, the laser scanner 12 shown in FIG. 2, is very similar to the laser scanner 10 of FIG. 1, with the exception of the incident and output laser beams. In this case, the incident laser beam 50 is collimated instead of focused. Collimated beams are reflected along paths 26 and 36, or some intermediate path, depending on the angle or position of the scanning mirror 16. The lens 18 refracts the collimated beams so that they focus at a focal plane 52 on the output side of the lens 18. The spots 54 and 56 of the pattern thus projected onto the target tissue are focused, small diameter spots. Again, the relative positioning of the spots within the

pattern does not change as a function of the separation distance between the lens **18** and the target tissue. The spot size does change somewhat as a function of the separation distance between the target tissue and the focal plane **52**, but the variation is not great, which allows for some movement of the laser scanner relative to the target tissue.

FIGS. **1** and **2** show how the invention works in one dimension. In the preferred embodiments, the laser scanner of the present invention produces a two-dimensional pattern by using a mirror or system of mirrors that project the laser beam onto the lens **18** in a two-dimensional pattern.

The laser scanner **10** is further illustrated in FIGS. **3–7**. As shown in FIG. **5**, the laser scanner **10** has two independently controlled mirrors **60, 62** that scans the laser beam in two orthogonal directions. Mirror **60** is mounted on a mirror mount **63** and is pivoted about axis **64** by a rotary galvanometer **66**. Mirror **62** is pivoted about an axis **68** by another rotary galvanometer **70**. The axes of rotation of the mirrors **60, 62** are mutually orthogonal and are also orthogonal to the incident laser beam **72**. The galvanometers **66, 70** are powered and controlled by a controller (not shown) that supplies appropriate voltages to the galvanometers to cause them and the attached mirrors to rotate to the desired positions. The two mirrors **60, 62** are separated by a small clearance to allow the two mirrors to move independently. The point **20**, which is one focal length away from the lens **18**, is located between the two mirrors, which causes a small deviation from the ideal situation where the mirrors would be coincident with point **20**.

The laser scanner **10** also includes a frame **74** and a cover **76** that houses the galvanometers **66** and **70**. An exit tube **78** is attached to the frame **74** and provides a mounting for lens **18**, a lens retainer **80**, a spacer **82**, a window **84**, and a window retainer **86**. At a distal end of the exit tube **78** is a smoke evacuation tip **88**, including an inner tube **90**, an outer sleeve **92**, and a port **94**. Also at the distal end of the assembly is a spatula **96**.

As shown in FIGS. **3** and **5**, the laser input end of the laser scanner **10** has an internally-threaded coupling **100** that attaches the laser scanner to the distal end **101** of an articulated arm **102** of a laser **103**. (FIG. **3** is not to scale). In the preferred embodiment, the laser beam is created by the Ultrapulse 5000, a carbon dioxide laser manufactured and sold by Coherent, Inc. The Ultrapulse 5000 produces a pulsed infrared laser beam having maximum specifications of 500 mJ per pulse, a pulse duration of up to 1 ms, at a repetition rate of 500 Hz, for an average power of 250 Watts.

As shown in FIG. **5**, between the coupling **100** and the mirrors **60, 62** are beam conditioning optics that focus the collimated input laser beam to the point **20**, which is one focal length of lens **18** away from the lens. The beam conditioning optics includes two lenses **104, 106** mounted in a telescope body **108**. Lens **106** is fixed and is mounted in a lens holder **110** and retained by a retainer **112**. Lens **104** is movable and is mounted in a lens holder **114** by a retainer **116**. The lens holder **114** is rotatably mounted within the telescope body **108**. A drive pin **118** is mounted to the inside of an adjustment knob **120** and engages a helical slot **122** in the outside of the lens holder **114**. The position of the lens **104** is adjusted by rotating the adjustment knob **120**. A guide pin **124** attached to the lens holder **114** rides in an axial slot in the telescope body **108** and prevents the lens holder **114** from rotating. As shown in FIG. **3**, the adjustment knob **120** is calibrated to indicate the approximate diameter of the spot of the output beam.

The design of the optics necessary to produce the desired beam dimensions will vary depending on the configuration

of optical elements used and the characteristics of the laser beam as it enters the handpiece. In the preferred embodiment of laser scanner **10**, lens **104** has a focal length of +50 mm, lens **106** has a focal length of -10 mm, and lens **18** has a focal length of +100 mm. The beam diameter of the laser beam supplied by laser **103** is about 6 mm. The output beam diameter is adjustable over the range of about 2 mm to 4 mm. The lens are preferably made from zinc selenide and the mirrors are preferably made from molybdenum. The lens **104** and **106** focus the laser beam to a spot diameter of about 0.5 mm at the scanning mirrors.

The construction of the other preferred embodiment of the present invention, laser scanner **12**, is shown in FIGS. **8–10**. Laser scanner **12** is similar in construction to laser scanner **10** (FIGS. **5–7**) except for the beam conditioning optics **140**. As shown in FIG. **8**, the beam conditioning optics **140** of laser scanner **12** has a body **142** that is mounted to the frame **74**. Lens **144** and **146** are retained in the body **142** by retainers **148** and **150**, respectively. The lenses **144, 146** reduce the diameter of the incoming laser beam **72** to a smaller diameter and supplies a collimated laser beam to the mirrors **60, 62**. The incoming laser beam **72** is collimated, so if its diameter is acceptable, then the lenses **144, 146** can be eliminated.

In the preferred embodiment of laser scanner **12**, lens **144** has a focal length of +50 mm, lens **146** has a focal length of -25 mm, and lens **18** has a focal length of +100 mm. The lenses **144** and **146** change the spot diameter of the incident laser beam from about 6 mm to about 3 mm at the point where the beam strikes the mirrors. The spot diameter of the output beam is about 0.5 mm at the focal plane **52**.

FIG. **4** illustrates a control panel **160** used with the laser scanner **10, 12**. The operator selects a numbered pattern by entering two digits with a key pad **162**. The pattern number is displayed by a display **164**. FIGS. **11** and **12** show various patterns that can be utilized with the laser scanner **10** or **12**, respectively. The operator also selects a percentage overlap by a key pad **166**. The overlap value is displayed by display **168**. A controller (not shown) uses the overlap value to adjust the relative spacing of the spots in the selected pattern to yield the desired overlap. The operator can also select on the control panel **160** using button **170** whether the pattern is to be delivered once or repeatedly, as indicated by indicators **172, 174**.

In operation, the operator selects a pattern, an overlap, and single/repeat scanning on the control panel **160** of the laser scanner. The operator also turns on the laser system and opens a manual safety shutter. A low-power visible beam supplied by the laser is used to aim the laser scanner on the target tissue. The operator then depresses a footswitch that causes the scanner to produce a complete treatment pattern by positioning the mirrors synchronously with the pulse rate of the laser beam. In other words, the mirrors are positioned for delivery of one spot when the first laser pulse arrives; then the mirrors are repositioned for delivery of the next spot when the next laser pulse arrives; and so on until the entire pattern is completed. If a single pattern is selected, the laser scanner stops after completing the pattern, even if the footswitch is still depressed. If a repeat pattern is selected, the treatment pattern will be repeated with a one-second delay between patterns until the footswitch is released. Early release of the footswitch in either single pattern or repeat pattern mode will terminate the treatment beam before the pattern is completed.

The above-described preferred embodiments utilize an axisymmetric lens **18** and two mirrors **60, 62** that are located

close to the point **20**, which is one focal length upstream from the lens **18**. This arrangement has a small error because the laser beam does not strike both mirrors at point **20**. Alternatively, a single mirror could be used along with a mechanism that would permit rotation in two dimensions about the point **20**. Also alternatively, the lens could be ground anamorphic, having two different focal lengths in two orthogonal planes. This would permit each of the two mirrors to be placed one focal length upstream from the lens without interfering with their independent movement. Such an anamorphic lens could have either a toroidal surface, or two opposed cylindrical surfaces located orthogonally on opposite sides of the lens.

Another alternative for the optics design would be to have a series of a first mirror, a first lens, a second mirror and a second lens. The first lens produces an image of the first mirror on top of the second mirror, and the second mirror is one focal length upstream from the second lens. The two mirrors appear to be in the same place, approximately one focal length from the second lens. Each mirror provides pattern deflection in one of two mutually orthogonal directions.

From the above description, it will be apparent that the invention disclosed herein provides a novel and advantageous surgical laser handpiece that scans a laser beam onto a target tissue. The foregoing discussion discloses and describes merely exemplary methods and embodiments of the present invention. As will be understood by those familiar with the art, the invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. Accordingly, the disclosure of the present invention is intended to be illustrative, but not limiting, of the scope of the invention, which is set forth in the following claims.

What is claimed is:

1. A surgical system for connection to a laser that generates a pulsed laser beam, wherein the surgical system scans the laser beam onto a target tissue, the surgical system comprising:

- a scanning mirror means for reflecting a pulsed laser beam;
- a lens onto which the scanning mirror means reflects the pulsed laser beam and through which the pulsed laser beam is refracted onto the target tissue; and
- a controller that operates the scanning mirror means to scan the pulses in the laser beam to form a selected pattern of spots on the target tissue, the controller being responsive to a control panel that includes:
 - a pattern selector for selecting the selected pattern from a plurality of predetermined patterns, and

an overlap selector for selecting the relative spacing between the spots in the selected pattern.

2. The surgical system as recited in claim **1**, wherein the lens is spaced from the scanning mirror means such that any variation in the size of the pattern on the target tissue is minimized as the spacing between the lens and the target tissue is varied.

3. The surgical system as recited in claim **2**, wherein the control panel further comprises:

- a repeat selector to cause the controller to scan the selected pattern onto the target tissue repeatedly.

4. The surgical system as recited in claim **2** further comprising:

- beam conditioning optics located between the laser and the scanning mirror means and including optical means for providing a focused beam to the scanning mirror means.

5. The surgical system as recited in claim **4**, wherein the optical means is movable to change the distance between the optical means and the scanning mirror which changes the size of the spots in the selected pattern.

6. The surgical system as recited in claim **5**, further comprising:

- an adjustment knob used to change the distance between the optical means and the scanning mirror, the adjustment knob having a visual indicator to indicate the approximate diameter of the spots in the selected pattern.

7. The surgical system of claim **2** wherein the scanning mirror means comprises two mirrors independently rotatable about two axes that are orthogonal to each other and orthogonal to the laser beam.

8. The surgical system of claim **7** wherein the scanning mirror means further comprises two galvanometers, wherein each galvanometer is coupled to one of the mirrors by a means that permits rotation of the mirror about an axis.

9. A surgical handpiece for connection to a laser that generates a laser beam, wherein the handpiece scans the laser beam onto a target tissue, the handpiece comprising:

- a scanning mirror means for reflecting the laser beam; and
- a lens onto which the scanning mirror reflects the laser beam and through which the laser beam is refracted onto the target tissue, wherein the lens has a focal length and the scanning mirror is located at a distance from the lens that is substantially equal to the focal length so that any variation in the size of a pattern projected onto the target tissue is minimized as the spacing between the lens and the target tissue is varied.

* * * * *